

NMCP COVID-19 Literature Report #66: Friday, 23 April 2021

Prepared By: Tracy C. Shields, MSIS, AHIP (Ms.; she/her) <tracy.c.shields2.civ@mail.mil>
Naval Medical Center Portsmouth; Library Services, Reference Medical Librarian

Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

TABLE OF CONTENTS

Topic page; click link to jump to section. References can be found on the website.

The Big Picture 2	Pediatric Population 24
SARS-CoV-2 Variants 3	Mental Health and Wellness 25
Vaccines and Vaccine Hesitancy 4	Disparities and Health Equity 28
Treatments and Management 9	Risk, Transmission, and Exposure 30
Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases 13	Impact on Healthcare Workers 34
Long COVID / Post-COVID Period 17	Reinfections, Coinfection, and Other Infectious Diseases 36
Women's Health, Pregnancy, and Perinatal Care 20	Statistics 38

The Big Picture

News in Brief

We have passed more than 3 million deaths from COVID-19 globally, as India is ravaged and setting world records for most cases in a day ([NPR](#)).

The US Government is pushing Congress to increase funding for public health and pandemic preparedness ([STAT](#)).

"We know a lot about Covid-19. Experts have many more questions" ([STAT](#)).

"To understand a global pandemic we need global data. But even more than one year into the pandemic some of the most basic international data on COVID is missing. Just because there is no international organization that brings this data together" ([@MaxCRoser](#); [full post via ThreadReader](#)).

Long Reads

"You won't remember the pandemic the way you think you will: The stories you hold on to will be colored by your own experience—but also by the experiences of those around you ([Atlantic](#)).

"The pandemic will likely end in one of these four ways " – better, mixed, worse, or worst ([BuzzFeed](#)).

"Vietnam defied the experts and sealed its border to keep Covid-19 out. It worked: How the country has kept coronavirus deaths to just 35, and grew its economy in 2020" ([Vox](#)).

Webinar

WHEN: Wednesday, 28 April 2021, 1100 ET

WHAT: Improving the Resilience of U.S. Health Care Systems for Future Pandemics

DETAILS: "Hospitals and health care systems are the life force behind an effective pandemic response in the United States. Yet during the COVID-19 pandemic, these public and private sector institutions experienced staff, supply, and equipment shortages; struggled with providing access to care in rural areas; and lacked data coordination. How can the federal government assist in tackling the problems experienced by these institutions during the COVID-19 pandemic to help them prepare for future pandemics and other health emergencies?"

REGISTER: https://jh.zoom.us/webinar/register/WN_Fe0WCAw-T9qpXRdVn2rUsw

Special Reports

GAO: [Global Health Security: USAID and CDC Funding, Activities, and Assessments of Countries' Capacities to Address Infectious Disease Threats before COVID-19 Onset](#) (published 14 April 2021)

"The US Government Accountability Office (GAO) released its findings of a study about the Global Health Security funds used US Agency for International Development (USAID) and the Centers for Disease Control and Prevention (CDC). USAID and the CDC invest in global health security to help other nations build their capacities to deal with infectious diseases. The GAO study found that USAID and the CDC had dispersed roughly \$1 billion as of 31 March 2020 for global health security activities. This money went to at least 34 countries, including 25 recognized as partner countries with the Global Health Security Agenda (GHS). This support helped build capacity in 17 GHS partner countries, which helps them address infectious disease threats. Also, by the end of fiscal year 2019, most of those 17 nations possessed some capacity in each of the 11 technical areas, but continued to face various challenge." (summary from [Pandora Report newsletter 23 April 2021](#))

SARS-CoV-2 Variants

News in Brief

A variant detected in Texas (BV-1) shows signs of antibody resistance and more severe illness in young people ([CNBC](#)).

An Israeli study suggests that the South Africa variant may 'break through' Pfizer vaccine protection ([Reuters](#); see: [medRxiv preprint](#); see also: [Twitter thread discussing the study](#)).

Curious about the variants in the US? See the CDC's COVID Tracker section on variants at: <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>

Peer-Reviewed Articles

NEJM: [Vaccine Breakthrough Infections with SARS-CoV-2 Variants](#) (21 April 2021)

"Emerging variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are of clinical concern. In a cohort of 417 persons who had received the second dose of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine at least 2 weeks previously, we identified 2 women with vaccine breakthrough infection. Despite evidence of vaccine efficacy in both women, symptoms of coronavirus disease 2019 developed, and they tested positive for SARS-CoV-2 by polymerase-chain-reaction testing. Viral sequencing revealed variants of likely clinical importance, including E484K in 1 woman and three mutations

(T95I, del142–144, and D614G) in both. These observations indicate a potential risk of illness after successful vaccination and subsequent infection with variant virus, and they provide support for continued efforts to prevent and diagnose infection and to characterize variants in vaccinated persons."

Vaccines and Vaccine Hesitancy

News in Brief

According to data from the CDC, "[f]or every 850 doses of Covid-19 vaccine administered by March 29, one dose had to be thrown out because it was 'unused, spoiled, expired, or wasted'" ([CNN](#)).

"A vaccine study in college students will help determine when it is safe to take masks off" ([WashPo](#); see also: [CoVPN Moderna study](#)).

China's CDC director admitted that the Chinese COVID-19 vaccines have lower effectiveness than mRNA vaccines ([AP](#)).

"The race to curb the spread of COVID vaccine disinformation: Researchers are applying strategies honed during the 2020 US presidential election to track anti-vax propaganda" ([Nature](#)).

Development and Production

Remember the huge batch of the J&J vaccine that had to be tossed because of contamination? ([ICYMI](#)) Well, the FDA inspected the facility and it has a lot of problems ([NPR](#)).

Sputnik V COVID-19 vaccine isn't the only one Russia has developed—EpiVacCorona has also been produced, but it's surrounded by mystery ([Science](#)).

Long read: "Kati Kariko helped shield the world from the coronavirus: collaborating with devoted colleagues, Dr. Kariko laid the groundwork for the mRNA vaccines turning the tide of the pandemic" ([NYT](#)).

Adverse Events: Coagulopathies

On Tuesday, 13 April 2021, the CDC and FDA released a statement that they were convening a meeting of Advisory Committee on Immunization Practices on Friday, 23 April 2021, to consider the potential significance of 6 known cases of blood clots after receiving the J&J vaccine ([FDA](#)).

"From VIPIT to VITT: Thrombosis and COVID vaccines — more data support link between adenovirus vector vaccines, blood clotting, and low platelets" ([MedPage Today](#)).

"The blood-clot problem is multiplying: So are theories to explain it" ([Atlantic](#)).

"How could a COVID vaccine cause blood clots? Scientists race to investigate: Researchers are searching for possible links between unusual clotting and the Oxford–AstraZeneca coronavirus vaccine" ([Nature](#)).

"Communicating the potential benefits and harms of the Astra-Zeneca COVID-19 vaccine" ([Univ of Cambridge](#)).

Podcast: "Could COVID vaccines cause blood clots? Here's what the science says" ([Nature](#)).

As concerning as all this is, COVID-19 – the actual disease – poses a greater threat for blood clots than vaccines ([CIDRAP](#); see also: [OSF preprint](#)).

Hesitancy

Up to 40% of Marines have declined the COVID-19 vaccine, with some locations even higher – for example, the declination rate at Camp Lejeune is 57% ([CNN](#)).

"1 in 5 Americans say they won't get COVID-19 vaccine" ([CIDRAP](#); see also: [poll results \[pdf\]](#)).

"How Israel persuaded reluctant ultra-orthodox Jews to get vaccinated against COVID-19" ([NPR](#)).

Commentary: "Rethinking vaccine hesitancy among minority groups"; of note: "Although vaccine hesitancy is often implicated, this framing mistakenly places the responsibility on minoritised groups to become less hesitant, rather than on public health systems to become more trustworthy and accessible" ([Lancet](#)).

Vaccination Cards and Passports

Fake and falsified vaccination cards are out there and could undermine pandemic recovery ([WashPo](#)).

What if you lose your card? Well, hopefully you've got a copy of it saved somewhere. Life Pro Tip: NMCP Library Services has a simple scanner that makes it easy to save as a pdf for your personal records ([WashPo](#)).

"Vaccine passports: 'Scarlet letter' or just the ticket?" ([NPR](#)).

Peer-Reviewed Articles

NEJM: [Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19](#) (21 April 2021)

"The Ad26.COV2.S vaccine is a recombinant, replication-incompetent human adenovirus type 26 vector encoding full-length severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein in a prefusion-stabilized conformation.

In an international, randomized, double-blind, placebo-controlled, phase 3 trial, we randomly assigned adult participants in a 1:1 ratio to receive a single dose of Ad26.COV2.S (5×10^{10} viral particles) or placebo. The primary end points were vaccine efficacy against moderate to severe–critical coronavirus disease 2019 (Covid-19) with an onset at least 14 days and at least 28 days after administration among participants in the per-protocol population who had tested negative for SARS-CoV-2. Safety was also assessed.

The per-protocol population included 19,630 SARS-CoV-2–negative participants who received Ad26.COV2.S and 19,691 who received placebo. Ad26.COV2.S protected against moderate to severe–critical Covid-19 with onset at least 14 days after administration (116 cases in the vaccine group vs. 348 in the placebo group; efficacy, 66.9%; adjusted 95% confidence interval [CI], 59.0 to 73.4) and at least 28 days after administration (66 vs. 193 cases; efficacy, 66.1%; adjusted 95% CI, 55.0 to 74.8). Vaccine efficacy was higher against severe–critical Covid-19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥ 14 days and 85.4% [adjusted 95% CI, 54.2 to 96.9] for onset at ≥ 28 days). Despite 86 of 91 cases (94.5%) in South Africa with sequenced virus having the 20H/501Y.V2 variant, vaccine efficacy was 52.0% and 64.0% against moderate to severe–critical Covid-19 with onset at least 14 days and at least 28 days after administration, respectively, and efficacy against severe–critical Covid-19 was 73.1% and 81.7%, respectively. Reactogenicity was higher with Ad26.COV2.S than with placebo but was generally mild to moderate and transient. The incidence of serious adverse events was balanced between the two groups. Three deaths occurred in the vaccine group (none were Covid-19–related), and 16 in the placebo group (5 were Covid-19–related).

A single dose of Ad26.COV2.S protected against symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection and was effective against severe–critical disease, including hospitalization and death. Safety appeared to be similar to that in other phase 3 trials of Covid-19 vaccines."

NEJM: [Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination](#) (16 April 2021)

"The mainstay of control of the coronavirus disease 2019 (Covid-19) pandemic is vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Within a year, several vaccines have been developed and millions of doses delivered. Reporting of adverse events is a critical postmarketing activity.

We report findings in 23 patients who presented with thrombosis and thrombocytopenia 6 to 24 days after receiving the first dose of the ChAdOx1 nCoV-19 vaccine (AstraZeneca). On the basis of their clinical and laboratory features, we identify a novel underlying mechanism and address the therapeutic implications.

In the absence of previous prothrombotic medical conditions, 22 patients presented with acute thrombocytopenia and thrombosis, primarily cerebral venous thrombosis, and 1 patient presented with isolated thrombocytopenia and a hemorrhagic phenotype. All the patients had low or normal fibrinogen levels and elevated d-dimer levels at presentation. No evidence of thrombophilia or causative precipitants was identified. Testing for antibodies to platelet factor 4 (PF4) was positive in 22 patients (with 1 equivocal result) and negative in 1 patient. On the basis of the pathophysiological features observed in these patients, we recommend that treatment with platelet transfusions be avoided because of the risk of progression in thrombotic symptoms and that the administration of a nonheparin anticoagulant agent and intravenous immune globulin be considered for the first occurrence of these symptoms.

Vaccination against SARS-CoV-2 remains critical for control of the Covid-19 pandemic. A pathogenic PF4-dependent syndrome, unrelated to the use of heparin therapy, can occur after the administration of the ChAdOx1 nCoV-19 vaccine. Rapid identification of this rare syndrome is important because of the therapeutic implications."

Rheumatology: [Herpes zoster following BNT162b2 mRNA Covid-19 vaccination in patients with autoimmune inflammatory rheumatic diseases: a case series](#) (12 April 2021)

"As global vaccination campaigns against COVID-19 disease commence, vaccine safety needs to be closely assessed. The safety profile of mRNA-based vaccines in patients with autoimmune inflammatory rheumatic diseases (AIIRD) is unknown. The objective of this report is to raise awareness to reactivation of herpes zoster (HZ) following the BNT162b2 mRNA vaccination in patients with AIIRD.

The safety of the BNT162b2 mRNA vaccination was assessed in an observational study monitoring post-vaccination adverse effects in patients with AIIRD (n = 491) and controls (n = 99), conducted in two Rheumatology Departments in Israel.

The prevalence of HZ was 1.2% (n = 6) in patients with AIIRD compared with none in controls. Six female patients aged 49 ± 11 years with stable AIIRD: rheumatoid arthritis (n = 4), Sjogren's syndrome (n = 1), and undifferentiated connective disease (n = 1), developed the first in a lifetime event of HZ within a short time after the first vaccine dose in 5 cases and after the second vaccine dose in one case. In the majority of cases, HZ infection was mild, except a case of HZ ophthalmicus, without corneal involvement, in RA patient treated with tofacitinib. There were no cases of disseminated HZ disease or postherpetic neuralgia. All but one patient received antiviral treatment with a resolution of HZ-related symptoms up to 6 weeks. Five patients completed the second vaccine dose without other adverse effects.

Epidemiologic studies on the safety of the mRNA-based COVID-19 vaccines in patients with AIIRD are needed to clarify the association between the BNT162b2 mRNA vaccination and reactivation of zoster."

NEJM: [Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination](#) (09 April 2021)

"Several cases of unusual thrombotic events and thrombocytopenia have developed after vaccination with the recombinant adenoviral vector encoding the spike protein antigen of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ChAdOx1 nCov-19, AstraZeneca). More data were needed on the pathogenesis of this unusual clotting disorder.

We assessed the clinical and laboratory features of 11 patients in Germany and Austria in whom thrombosis or thrombocytopenia had developed after vaccination with ChAdOx1 nCov-19. We used a standard enzyme-linked immunosorbent assay to detect platelet factor 4 (PF4)–heparin antibodies and a modified (PF4-enhanced) platelet-activation test to detect platelet-activating antibodies under various reaction conditions. Included in this testing were samples from patients who had blood samples referred for investigation of vaccine-associated thrombotic events, with 28 testing positive on a screening PF4–heparin immunoassay.

Of the 11 original patients, 9 were women, with a median age of 36 years (range, 22 to 49). Beginning 5 to 16 days after vaccination, the patients presented with one or more thrombotic events, with the exception of 1 patient, who presented with fatal intracranial hemorrhage. Of the patients with one or more thrombotic events, 9 had cerebral venous thrombosis, 3 had splanchnic-vein thrombosis, 3 had pulmonary embolism, and 4 had other thromboses; of these patients, 6 died. Five patients had disseminated intravascular coagulation. None of the patients had received heparin before symptom onset. All 28 patients who tested positive for antibodies against PF4–heparin tested positive on the platelet-activation assay in the presence of PF4 independent of heparin. Platelet activation was inhibited by high levels of heparin, Fc receptor–blocking monoclonal antibody, and immune globulin (10 mg per milliliter). Additional studies with PF4 or PF4–heparin affinity purified antibodies in 2 patients confirmed PF4-dependent platelet activation.

Vaccination with ChAdOx1 nCov-19 can result in the rare development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia."

NEJM: [Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination](#) (09 April 2021)

"We report findings in five patients who presented with venous thrombosis and thrombocytopenia 7 to 10 days after receiving the first dose of the ChAdOx1 nCoV-19 adenoviral vector vaccine against coronavirus disease 2019 (Covid-19). The patients were

health care workers who were 32 to 54 years of age. All the patients had high levels of antibodies to platelet factor 4–polyanion complexes; however, they had had no previous exposure to heparin. Because the five cases occurred in a population of more than 130,000 vaccinated persons, we propose that they represent a rare vaccine-related variant of spontaneous heparin-induced thrombocytopenia that we refer to as vaccine-induced immune thrombotic thrombocytopenia."

Elife: [Single-dose BNT162b2 vaccine protects against asymptomatic SARS-CoV-2 infection](#) (08 April 2021)

"The BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) is being utilised internationally for mass COVID-19 vaccination. Evidence of single-dose protection against symptomatic disease has encouraged some countries to opt for delayed booster doses of BNT162b2, but the effect of this strategy on rates of asymptomatic SARS-CoV-2 infection remains unknown. We previously demonstrated frequent pauci- and asymptomatic SARS-CoV-2 infection amongst healthcare workers (HCWs) during the UK's first wave of the COVID-19 pandemic, using a comprehensive PCR-based HCW screening programme (Rivett et al., 2020; Jones et al., 2020). Here, we evaluate the effect of first-dose BNT162b2 vaccination on test positivity rates, and find a four-fold reduction in asymptomatic infection amongst HCWs ≥ 12 days post-vaccination. These data provide real-world evidence of short-term protection against asymptomatic SARS-CoV-2 infection following a single dose of BNT162b2 vaccine, suggesting that mass first-dose vaccination will reduce SARS-CoV-2 transmission, as well as the burden of COVID-19 disease."

Treatments and Management

News in Brief

On 21 April 2021, the NIH updated its COVID-19 treatment guidelines, including: new sections on outpatient management of acute COVID-19, colchicine, and fluvoxamine; and key updates on therapeutic management of adults, the clinical spectrum of infection, monoclonal antibodies, convalescent plasma, and special considerations in children. For more details, see: <https://www.covid19treatmentguidelines.nih.gov/whats-new/>

As of 16 April 2021, the FDA has revoked the EUA for bamlanivimab when used alone: "Based on its ongoing analysis of emerging scientific data, specifically the sustained increase of SARS-CoV-2 viral variants that are resistant to bamlanivimab alone resulting in the increased risk for treatment failure, the FDA has determined that the known and potential benefits of bamlanivimab, when administered alone, no longer outweigh the known and potential risks for its authorized use" ([FDA](#)).

Drug Developments

"Scientists work toward an elusive dream: a simple pill to treat Covid-19" ([STAT](#)).

Merck's antiviral pill had 'encouraging' results but failed to help hospitalized patients ([STAT](#)).

"Regeneron says antibody cocktail prevented Covid when given as simple injection, not an IV" ([STAT](#)).

As part of the ACTIV protocol, the NIH will study repurposed drugs (the list is still being finalized) for potential treatment of COVID-19 ([NIH](#)).

Long read: "The race for antiviral drugs to beat COVID — and the next pandemic: Despite dire warnings, a stockpile of ready compounds to fight viral pandemics was sorely lacking. Can drugmakers finally do the right thing?" ([Nature](#))

Peer-Reviewed Articles

JAMA Netw Open: [Effect of Early Treatment With Hydroxychloroquine or Lopinavir and Ritonavir on Risk of Hospitalization Among Patients With COVID-19: The TOGETHER Randomized Clinical Trial](#) (22 April 2021)

"Question: Does hydroxychloroquine or lopinavir-ritonavir, administered as a 9-day course, prevent COVID-19–associated hospitalization in patients with COVID-19?

Findings: In this trial that included 685 patients, rates of COVID-19–associated hospitalization in patients treated with hydroxychloroquine or lopinavir-ritonavir were not significantly different compared with those who received placebo.

Meaning: These findings may inform COVID-19 treatment guidelines for outpatients with COVID-19 and demonstrate that large-scale outpatient clinical trials of repurposed drugs can be successfully completed in low-income settings during the pandemic."

Clin Infect Dis: [Impact of convalescent plasma therapy on SARS CoV-2 antibody profile in COVID-19 patients](#) (16 April 2021)

"Convalescent plasma (CP) have been used for treatment of COVID-19, but their effectiveness varies significantly. Moreover, the impact of CP treatment on the composition of SARS-CoV-2 antibodies in COVID-19 patients and antibody markers that differentiate between those who survive and those who succumb to the COVID-19 disease are not well understood. Herein, we performed longitudinal analysis of antibody profile on 115 sequential plasma samples from 16 hospitalized COVID-19 patients treated with either CP or standard of care, only half of them survived. Differential antibody kinetics was observed for antibody binding, IgM/IgG/IgA distribution, and affinity maturation in 'survived' vs. 'fatal'

COVID-19 patients. Surprisingly, CP treatment did not predict survival. Strikingly, marked decline in neutralization titers was observed in the fatal patients prior to death, and convalescent plasma treatment did not reverse this trend. Furthermore, irrespective of CP treatment, higher antibody affinity to the SARS-CoV-2 prefusion spike was associated with survival outcome, while sustained elevated IgA response was associated with fatal outcome in these COVID-19 patients. These findings propose that treatment of COVID-19 patients with convalescent plasma should be carefully targeted, and effectiveness of treatment may depend on the clinical and immunological status of COVID-19 patients as well as the quality of the antibodies in the convalescent plasma."

Clin Infect Dis: [Real-World Experience of Bamlanivimab for COVID-19: A Case-Control Study](#) (13 April 2021)

"COVID-19 has strained healthcare systems with patient hospitalizations and deaths. Anti-spike monoclonal antibodies, including bamlanivimab, have demonstrated reduction in hospitalization rates in clinical trials, yet real-world evidence is lacking.

We conducted a retrospective case-control study across a single healthcare system of non-hospitalized patients, age 18 years or older, with documented positive SARS-CoV-2 testing, risk factors for severe COVID-19, and referrals for bamlanivimab via emergency use authorization. Cases were defined as patients who received bamlanivimab; contemporary controls had a referral order placed but did not receive bamlanivimab. The primary outcome was 30-day hospitalization rate from initial positive SARS-CoV-2 PCR. Descriptive statistics, including Chi-square and Mann-Whitney U test, were performed. Multivariable logistic regression was used for adjusted analysis to evaluate independent associations with 30-day hospitalization.

Between November 20, 2020 and January 19, 2021, 218 patients received bamlanivimab (cases) and 185 were referred but did not receive drug (controls). Thirty-day hospitalization rate was significantly lower among patients who received bamlanivimab (7.3% v 20.0%, RR 0.37, 95% CI 0.21-0.64, $p < 0.001$), and the number needed to treat was 8. On logistic regression, odds of hospitalization were increased in patients not receiving bamlanivimab and with a higher number of pre-specified comorbidities (OR 4.19 CI: 1.31-2.16, $p < 0.001$; OR 1.68, CI: 2.12-8.30, $p < 0.001$, respectively).

Ambulatory patients with COVID-19 who received bamlanivimab had a lower 30-day hospitalization than control patients in real-world experience. We identified receipt of bamlanivimab and fewer comorbidities as protective factors against hospitalization."

Ann Surg: [Analysis of COVID-19 Patients with Acute Respiratory Distress Syndrome Managed with Extracorporeal Membrane Oxygenation at us Academic Centers](#) (09 April 2021)

"This study analyzed the outcomes of COVID-19 patients with ARDS who were managed with extracorporeal membrane oxygenation (ECMO) across 155 US academic centers.

ECMO has been utilized in COVID-19 patients with acute respiratory distress syndrome (ARDS) and refractory hypoxemia. Early case series with the use of ECMO in these patients reported high mortality exceeding 90%.

Using ICD-10 codes, data of patients with COVID-19 with ARDS, managed with ECMO between April - September 2020 were analyzed using the Vizient clinical database. Outcomes measured included in-hospital mortality, hospital and ICU length of stay (LOS) and direct cost. For comparative purposes, the outcome of a subset of COVID-19 patients aged between 18–64 years and managed with vs. without ECMO were examined.

1,1182 patients with COVID-19 and ARDS received ECMO. In-hospital mortality was 45.9%, mean LOS was 36.8 ± 24.9 days and mean ICU stay was 29.1 ± 17.3 days. In-hospital mortality, according to age group was 25.2% for 1-30 years; 42.2% for 31–50 years; 53.2% for 51–64 years; and 73.7% for ≥ 65 years. A subset analysis of COVID-19 patients, aged 18–64 years with ARDS requiring mechanical ventilation and managed with (n = 1113) vs without (n = 16,343) ECMO, showed relatively high in-hospital mortality for both groups (44.6% with ECMO vs 37.9% without ECMO).

In this large US study of patients with COVID-19 and ARDS managed with ECMO, the in-hospital mortality is high but much lower than initial reports. Future research is needed to evaluate which patients with COVID-19 and ARDS would benefit from ECMO."

Crit Care: [Effect of timing of intubation on clinical outcomes of critically ill patients with COVID-19: a systematic review and meta-analysis of non-randomized cohort studies](#) (25 March 2021)

"Although several international guidelines recommend early over late intubation of patients with severe coronavirus disease 2019 (COVID-19), this issue is still controversial. We aimed to investigate the effect (if any) of timing of intubation on clinical outcomes of critically ill patients with COVID-19 by carrying out a systematic review and meta-analysis.

PubMed and Scopus were systematically searched, while references and preprint servers were explored, for relevant articles up to December 26, 2020, to identify studies which reported on mortality and/or morbidity of patients with COVID-19 undergoing early versus late intubation. "Early" was defined as intubation within 24 h from intensive care unit (ICU) admission, while "late" as intubation at any time after 24 h of ICU admission. All-cause mortality and duration of mechanical ventilation (MV) were the primary outcomes of the meta-analysis. Pooled risk ratio (RR), pooled mean difference (MD) and 95% confidence intervals (CI) were calculated using a random effects model. The meta-analysis was registered with PROSPERO (CRD42020222147).

A total of 12 studies, involving 8944 critically ill patients with COVID-19, were included. There was no statistically detectable difference on all-cause mortality between patients undergoing early versus late intubation (3981 deaths; 45.4% versus 39.1%; RR 1.07, 95% CI 0.99–1.15, $p = 0.08$). This was also the case for duration of MV (1892 patients; MD – 0.58 days, 95% CI – 3.06 to 1.89 days, $p = 0.65$). In a sensitivity analysis using an alternate definition of early/late intubation, intubation without versus with a prior trial of high-flow nasal cannula or noninvasive mechanical ventilation was still not associated with a statistically detectable difference on all-cause mortality (1128 deaths; 48.9% versus 42.5%; RR 1.11, 95% CI 0.99–1.25, $p = 0.08$).

The synthesized evidence suggests that timing of intubation may have no effect on mortality and morbidity of critically ill patients with COVID-19. These results might justify a wait-and-see approach, which may lead to fewer intubations. Relevant guidelines may therefore need to be updated."

Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

News in Brief

"After a year of pandemic-delayed medical treatments, doctors are seeing more cases of advanced illnesses" ([WashPo](#)).

Peer-Reviewed Articles

BMJ Nutr Prev Health: [Modest effects of dietary supplements during the COVID-19 pandemic: insights from 445 850 users of the COVID-19 Symptom Study app](#) (19 April 2021)

"Objectives: Dietary supplements may ameliorate SARS-CoV-2 infection, although scientific evidence to support such a role is lacking. We investigated whether users of the COVID-19 Symptom Study app who regularly took dietary supplements were less likely to test positive for SARS-CoV-2 infection.

Setting 445 850 subscribers of an app that was launched to enable self-reported information related to SARS-CoV-2 infection for use in the general population in the UK ($n=372\,720$), the USA ($n=45\,757$) and Sweden ($n=27\,373$).

Results: In 372 720 UK participants (175 652 supplement users and 197 068 non-users), those taking probiotics, omega-3 fatty acids, multivitamins or vitamin D had a lower risk of SARS-CoV-2 infection by 14% (95% CI (8% to 19%)), 12% (95% CI (8% to 16%)), 13% (95% CI (10% to 16%)) and 9% (95% CI (6% to 12%)), respectively, after adjusting for potential confounders. No effect was observed for those taking vitamin C, zinc or garlic supplements.

On stratification by sex, age and body mass index (BMI), the protective associations in individuals taking probiotics, omega-3 fatty acids, multivitamins and vitamin D were observed in females across all ages and BMI groups, but were not seen in men. The same overall pattern of association was observed in both the US and Swedish cohorts.

Conclusion: In women, we observed a modest but significant association between use of probiotics, omega-3 fatty acid, multivitamin or vitamin D supplements and lower risk of testing positive for SARS-CoV-2. We found no clear benefits for men nor any effect of vitamin C, garlic or zinc. Randomised controlled trials are required to confirm these observational findings before any therapeutic recommendations can be made."

Diabetes Care: [Diabetes and Overweight/Obesity Are Independent, Nonadditive Risk Factors for In-Hospital Severity of COVID-19: An International, Multicenter Retrospective Meta-analysis](#) (15 April 2021)

"We retrospectively extracted data from health care records and regional databases of hospitalized adult patients with COVID-19 from 18 sites in 11 countries. We used standardized definitions and analyses to generate site-specific estimates, modeling the odds of each outcome (supplemental oxygen/noninvasive ventilatory support, invasive mechanical ventilatory support, and in-hospital mortality) by BMI category (reference, overweight, obese), adjusting for age, sex, and prespecified comorbidities. Subgroup analysis was performed on patients with preexisting diabetes. Site-specific estimates were combined in a meta-analysis.

Among 7,244 patients (65.6% overweight/obese), those with overweight were more likely to require oxygen/noninvasive ventilatory support (random effects adjusted odds ratio [aOR], 1.44; 95% CI 1.15–1.80) and invasive mechanical ventilatory support (aOR, 1.22; 95% CI 1.03–1.46). There was no association between overweight and in-hospital mortality (aOR, 0.88; 95% CI 0.74–1.04). Similar effects were observed in patients with obesity or diabetes. In the subgroup analysis, the aOR for any outcome was not additionally increased in those with diabetes and overweight or obesity.

In adults hospitalized with COVID-19, overweight, obesity, and diabetes were associated with increased odds of requiring respiratory support but were not associated with death. In patients with diabetes, the odds of severe COVID-19 were not increased above the BMI-associated risk."

JAMA Netw Open: [Prescribing of Opioid Analgesics and Buprenorphine for Opioid Use Disorder During the COVID-19 Pandemic](#) (15 April 2021)

"Question: How has prescribing of opioid analgesics and buprenorphine for opioid use disorder changed throughout the COVID-19 pandemic?

Findings: This cross-sectional study analyzed prescriptions from 90 420 353 patients and found that from March 18 to May 19, 2020, total morphine milligram equivalents of opioid analgesics prescribed to existing patients followed prepandemic trends; prescriptions to opioid-naïve patients were 34% below projected levels but rebounded by August 2020. Prescribing of buprenorphine for opioid use disorder followed prepandemic trends for existing patients, while prescriptions to new patients were 18% below projected levels, rebounding to 90% of projected levels by August 2020.

Meaning: This study suggests that prescriptions for opioid analgesics and buprenorphine for opioid use disorder decreased among new, but not existing, patients during the COVID-19 pandemic."

Br J Sport Med: [Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients](#) (13 April 2021)

"To compare hospitalisation rates, intensive care unit (ICU) admissions and mortality for patients with COVID-19 who were consistently inactive, doing some activity or consistently meeting physical activity guidelines.

We identified 48 440 adult patients with a COVID-19 diagnosis from 1 January 2020 to 21 October 2020, with at least three exercise vital sign measurements from 19 March 2018 to 18 March 2020. We linked each patient's self-reported physical activity category (consistently inactive=0–10 min/week, some activity=11–149 min/week, consistently meeting guidelines=150+ min/week) to the risk of hospitalisation, ICU admission and death after COVID-19 diagnosis. We conducted multivariable logistic regression controlling for demographics and known risk factors to assess whether inactivity was associated with COVID-19 outcomes.

Patients with COVID-19 who were consistently inactive had a greater risk of hospitalisation (OR 2.26; 95% CI 1.81 to 2.83), admission to the ICU (OR 1.73; 95% CI 1.18 to 2.55) and death (OR 2.49; 95% CI 1.33 to 4.67) due to COVID-19 than patients who were consistently meeting physical activity guidelines. Patients who were consistently inactive also had a greater risk of hospitalisation (OR 1.20; 95% CI 1.10 to 1.32), admission to the ICU (OR 1.10; 95% CI 0.93 to 1.29) and death (OR 1.32; 95% CI 1.09 to 1.60) due to COVID-19 than patients who were doing some physical activity.

Consistently meeting physical activity guidelines was strongly associated with a reduced risk for severe COVID-19 outcomes among infected adults. We recommend efforts to promote physical activity be prioritised by public health agencies and incorporated into routine medical care."

JAMA Netw Open: [Postoperative In-Hospital Morbidity and Mortality of Patients With COVID-19 Infection Compared With Patients Without COVID-19 Infection](#) (12 April 2021)

"This cohort study uses the Vizient Clinical Data Base to compare the postoperative in-hospital morbidity and mortality of surgical patients with COVID-19 infection with patients without COVID-19 infection....

A total of 5470 surgical patients with positive COVID-19 test results were matched with 5470 surgical patients with negative COVID-19 test results during the same study period. Among all hospitals, there were more than double the number of deaths reported in the cohort of patients with COVID-19 (811 [14.8%]) compared with the cohort of patients without COVID-19 (388 [7.1%]) ($P < .001$)."

JAMA Netw Open: [Model-Based Estimation of Colorectal Cancer Screening and Outcomes During the COVID-19 Pandemic](#) (12 April 2021)

"Question: What 3-year clinical outcomes are associated with expanding fecal immunochemical test (FIT)–based colorectal cancer screening participation during the COVID-19 pandemic?

Findings: In this modeling study, increasing FIT use from 15% to 22% over a 3-year period to offset COVID-19–related declines in colonoscopy screening was associated with an additional 655 825 colorectal cancer screenings and 2715 colorectal cancer diagnoses, of which 72% were early stage.

Meaning: These findings suggest that increasing FIT use for colorectal cancer screening during the COVID-19 pandemic may mitigate the consequences of reduced screening rates caused by the pandemic for colorectal cancer outcomes."

J Am Soc Nephrol: [Initial Effects of COVID-19 on Patients with ESKD](#) (08 April 2021)

"Although reports from around the world have indicated the case fatality rate of novel coronavirus disease 2019 (COVID-19) among patients with ESKD is between 20% and 30%, the population-level effect of COVID-19 is uncertain. In a retrospective analysis of data from the Centers for Medicare and Medicaid Services, during epidemiologic weeks 13–27 of 2020, adjusted relative rates of death were 17% higher among patients undergoing dialysis, and 30% higher among patients with a kidney transplant relative to corresponding weeks in 2017 to 2019. COVID-19 hospitalization rates and excess mortality both exhibited racial disparities. The severe effects of COVID-19 on patients with ESKD should be considered in the prioritization of these patients for COVID-19 vaccination."

Clin Rheumatol: [Are antiphospholipid antibodies just a common epiphenomenon or are they causative of immune-mediated coagulopathy in COVID-19?](#) (07 April 2021)

"The coronavirus disease 2019 (COVID-19) is the largest public health emergency in recent times. A significant number of patients develop a severe form of COVID-19 characterized by coagulopathy, organ failure, and elevated mortality. In addition, an unusually high

frequency of antiphospholipid antibodies (aPLs) has been found in patients with COVID-19. These clinical and serological manifestations closely resemble those seen in the antiphospholipid syndrome (APS), especially in its catastrophic form, suggesting a role of aPLs in immune-associated coagulopathy. However, government bodies such as the American Society of Hematology have spoken out against the systematic search for aPLs in patients with COVID-19. In an attempt to bridge the gap on this hot topic, we conducted a comprehensive review of currently available cohort studies and case series systematically evaluating aPLs in COVID-19 patients. In this Perspective, we seek to identify both the frequency and the type of aPLs found in patients with COVID-19, as well as the potential association of these aPLs with vascular thrombosis and other distinctive characteristics of COVID-19. Furthermore, we investigated whether there is evidence that allows us to define the occurrence of aPLs in COVID-19 as an epiphenomenon, as has been observed in other systemic viral infections, or as antibodies against self-antigens bearing hallmarks that suggest a pathogenic role in immune-mediated thrombosis. Defining whether aPLs represent an epiphenomenon or they are actually involved in hemostatic abnormalities of COVID-19 is crucial both for uncovering novel mechanisms of immune-mediated thrombosis and for identifying potential prognostic biomarkers in this devastating disease."

Minerva Anestesiol: [Statin therapy is associated with less ICU admissions in COVID-19 patients. A preliminary analysis of the current observations](#) (10 March 2021)

"We aimed to determine whether prior use of statins might affect the risk of admission in intensive care unit (ICU) of COVID-19 patients, by meta-analysing the available observations on this issue....

Our brief analysis suggests the potential protective effect of prior statin therapy, by reducing the risk of ICU admission of 15% in COVID-19 patients. From a pathophysiological perspective, this effect could be due to several mechanisms such as up-regulation of ACE2 receptor, reducing cytokines and by preventing, at least partially, the cardiological complications related to COVID-19 and requiring ICU admission."

Long COVID / Post-COVID Period

News in Brief

"The way out of brain fog: One of COVID-19's most persistent and mysterious problems finally has some treatments" ([Atlantic](#)).

"No one was listening': Long Covid patients struggle to get care for their symptoms" ([STAT](#)).

"Long COVID's long R&D agenda: As researchers work to understand the biology and epidemiology of post-acute COVID-19, a pioneering platform trial is now testing treatments to

try to address the long-term complications of infection in previously hospitalized individuals" ([Nature](#)).

"How scientists are teasing apart the biology of Long COVID" ([Science](#)).

Opinion: "Needed for long Covid: a less authoritarian approach to understanding, treatment" ([STAT](#)).

Long read: "Long Covid isn't as unique as we thought: The nagging symptoms long-haulers experience reveal a frustrating blind spot in medicine" ([Vox](#)).

Peer-Reviewed Articles

MMWR: [Health Care Utilization and Clinical Characteristics of Nonhospitalized Adults in an Integrated Health Care System 28–180 Days After COVID-19 Diagnosis — Georgia, May 2020–March 2021](#) (23 April 2021)

"What is already known about this topic? Health care needs in the months after a COVID-19 diagnosis among nonhospitalized adults have not been well studied.

What is added by this report? Among 3,171 nonhospitalized adult COVID-19 patients, 69% had one or more outpatient visits 28–180 days after the diagnosis. Two thirds had a visit for a new primary diagnosis, and approximately one third had a new specialist visit. Symptoms potentially related to COVID-19 were common new visit diagnoses. Visits for these symptoms decreased after 60 days but for some patients continued through 120–180 days.

What are the implications for public health practice? Clinicians and health care systems should be aware of the potential for post-COVID conditions."

Nature: [High-dimensional characterization of post-acute sequelae of COVID-19](#) (22 April 2021)

"The acute clinical manifestations of COVID-19 are well characterized^{1,2}; however, its post-acute sequelae have not been comprehensively described. Here, we use the national healthcare databases of the US Department of Veterans Affairs to systematically and comprehensively identify 6-month incident sequelae including diagnoses, medication use, and laboratory abnormalities in 30-day survivors of COVID-19. We show that beyond the first 30 days of illness, people with COVID-19 exhibit higher risk of death and health resource utilization. Our high dimensional approach identifies incident sequelae in the respiratory system and several others including nervous system and neurocognitive disorders, mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders, malaise, fatigue, musculoskeletal pain, and anemia. We show increased incident use of several therapeutics including pain medications (opioids and non-opioids), antidepressants, anxiolytics, antihypertensives, and oral hypoglycemics and

evidence of laboratory abnormalities in multiple organ systems. Analysis of an array of pre-specified outcomes reveals a risk gradient that increased across severity of the acute COVID-19 infection (non-hospitalized, hospitalized, admitted to intensive care). The findings show that beyond the acute illness, substantial burden of health loss — spanning pulmonary and several extrapulmonary organ systems — is experienced by COVID-19 survivors. The results provide a roadmap to inform health system planning and development of multidisciplinary care strategies to reduce chronic health loss among COVID-19 survivors."

Brain: [COVID-19 neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital](#) (15 April 2021)

"Many patients with SARS-CoV-2 infection develop neurological signs and symptoms, though, to date, little evidence exists that primary infection of the brain is a significant contributing factor. We present the clinical, neuropathological, and molecular findings of 41 consecutive patients with SARS-CoV-2 infections who died and underwent autopsy in our medical center. The mean age was 74 years (38–97 years), 27 patients (66%) were male and 34 (83%) were of Hispanic/Latinx ethnicity. Twenty-four patients (59%) were admitted to the intensive care unit (ICU). Hospital-associated complications were common, including 8 (20%) with deep vein thrombosis/pulmonary embolism (DVT/PE), 7 (17%) patients with acute kidney injury requiring dialysis, and 10 (24%) with positive blood cultures during admission. Eight (20%) patients died within 24 hours of hospital admission, while 11 (27%) died more than 4 weeks after hospital admission. Neuropathological examination of 20–30 areas from each brain revealed hypoxic/ischemic changes in all brains, both global and focal; large and small infarcts, many of which appeared hemorrhagic; and microglial activation with microglial nodules accompanied by neuronophagia, most prominently in the brainstem. We observed sparse T lymphocyte accumulation in either perivascular regions or in the brain parenchyma. Many brains contained atherosclerosis of large arteries and arteriolosclerosis, though none had evidence of vasculitis. Eighteen (44%) contained pathologies of neurodegenerative diseases, not unexpected given the age range of our patients. We examined multiple fresh frozen and fixed tissues from 28 brains for the presence of viral RNA and protein, using quantitative reverse-transcriptase PCR (qRT-PCR), RNAscope, and immunocytochemistry with primers, probes, and antibodies directed against the spike and nucleocapsid regions. qRT-PCR revealed low to very low, but detectable, viral RNA levels in the majority of brains, although they were far lower than those in nasal epithelia. RNAscope and immunocytochemistry failed to detect viral RNA or protein in brains. Our findings indicate that the levels of detectable virus in COVID-19 brains are very low and do not correlate with the histopathological alterations. These findings suggest that microglial activation, microglial nodules and neuronophagia, observed in the majority of brains, do not result from direct viral infection of brain parenchyma, but rather likely from systemic inflammation, perhaps with synergistic contribution from hypoxia/ischemia.

Further studies are needed to define whether these pathologies, if present in patients who survive COVID-19, might contribute to chronic neurological problems."

Women's Health, Pregnancy, and Perinatal Care

News in Brief

"No, we don't know if vaccines change your period: We do know that researchers do not study menstruation enough" ([NYT](#)).

If you've gotten at least one dose of a COVID-19 vaccine, menstruate, and want to help with that particular research gap, there's a survey you can participate in from Dr. Kathryn Clancy, Department of Anthropology, University of Illinois at Urbana-Champaign; see:

<https://redcap.healthinstitute.illinois.edu/surveys/index.php?s=LL8TKKC8DP>

Peer-Reviewed Articles

JAMA Pediatr: [Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study](#) (22 April 2021)

"Question: To what extent does COVID-19 in pregnancy alter the risks of adverse maternal and neonatal outcomes compared with pregnant individuals without COVID-19?

Findings: In this multinational cohort study of 2130 pregnant women in 18 countries, women with COVID-19 diagnosis were at increased risk of a composite maternal morbidity and mortality index. Newborns of women with COVID-19 diagnosis had significantly higher severe neonatal morbidity index and severe perinatal morbidity and mortality index compared with newborns of women without COVID-19 diagnosis.

Meaning: This study indicates a consistent association between pregnant individuals with COVID-19 diagnosis and higher rates of adverse outcomes, including maternal mortality, preeclampsia, and preterm birth compared with pregnant individuals without COVID-19 diagnosis."

NEJM: [Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons](#) (21 April 2021)

"Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy.

From December 14, 2020, to February 28, 2021, we used data from the "v-safe after vaccination health checker" surveillance system, the v-safe pregnancy registry, and the

Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons.

A total of 35,691 v-safe participants 16 to 54 years of age identified as pregnant. Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. Among 3958 participants enrolled in the v-safe pregnancy registry, 827 had a completed pregnancy, of which 115 (13.9%) resulted in a pregnancy loss and 712 (86.1%) resulted in a live birth (mostly among participants with vaccination in the third trimester). Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%); no neonatal deaths were reported. Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases).

Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes."

PLoS One: [A cross-national study of factors associated with women's perinatal mental health and wellbeing during the COVID-19 pandemic](#) (21 April 2021)

"Pregnant and postpartum women face unique challenges during the COVID-19 pandemic that may put them at elevated risk of mental health problems. However, few large-scale and no cross-national studies have been conducted to date that investigate modifiable pandemic-related behavioral or cognitive factors that may influence mental health in this vulnerable group. This international study sought to identify and measure the associations between pandemic-related information seeking, worries, and prevention behaviors on perinatal mental health during the COVID-19 pandemic.

An anonymous, online, cross-sectional survey of pregnant and postpartum women was conducted in 64 countries between May 26, 2020 and June 13, 2020. The survey, available in twelve languages, was hosted on the Pregistry platform for COVID-19 studies (<https://corona.pregistry.com>) and advertised in social media channels and online parenting forums.

Participants completed measures on demographics, COVID-19 exposure and worries, information seeking, COVID-19 prevention behaviors, and mental health symptoms including posttraumatic stress via the IES-6, anxiety/depression via the PHQ-4, and loneliness via the UCLA-3. Of the 6,894 participants, substantial proportions of women

scored at or above the cut-offs for elevated posttraumatic stress (2,979 [43%]), anxiety/depression (2,138 [31%], and loneliness (3,691 [53%]). Information seeking from any source (e.g., social media, news, talking to others) five or more times per day was associated with more than twice the odds of elevated posttraumatic stress and anxiety/depression, in adjusted models.

A majority of women (86%) reported being somewhat or very worried about COVID-19. The most commonly reported worries were related to pregnancy and delivery, including family being unable to visit after delivery (59%), the baby contracting COVID-19 (59%), lack of a support person during delivery (55%), and COVID-19 causing changes to the delivery plan (41%). Greater worries related to children (i.e., inadequate childcare, their infection risk) and missing medical appointments were associated with significantly higher odds of posttraumatic stress, anxiety/depression and loneliness. Engaging in hygiene-related COVID-19 prevention behaviors (face mask-wearing, washing hands, disinfecting surfaces) were not related to mental health symptoms or loneliness.

Elevated posttraumatic stress, anxiety/depression, and loneliness are highly prevalent in pregnant and postpartum women across 64 countries during the COVID-19 pandemic. Excessive information seeking and worries related to children and medical care are associated with elevated symptoms, whereas engaging in hygiene-related preventive measures were not. In addition to screening and monitoring mental health symptoms, addressing excessive information seeking and women's worries about access to medical care and their children's well-being, and developing strategies to target loneliness (e.g., online support groups) should be part of intervention efforts for perinatal women.

Public health campaigns and medical care systems need to explicitly address the impact of COVID-19 related stressors on mental health in perinatal women, as prevention of viral exposure itself does not mitigate the pandemic's mental health impact."

JAMA Netw Open: [Comparison Between In-Person and Audio-Only Virtual Prenatal Visits and Perinatal Outcomes](#) (14 April 2021)

"Question: Were audio-only virtual prenatal visits during the COVID-19 pandemic associated with a change in perinatal outcomes in a vulnerable population?

Findings: In this cohort study of 12 607 women, 173 women (2.9%) experienced placental abruption, stillbirth, cord pH less than 7.0, or full-term neonatal intensive care unit admission, which was not significantly different than the 195 women (3.0%) affected in 2019. The rate of this composite outcome also did not differ significantly when stratified by the number of virtual prenatal visits.

Meaning: In this study, women who delivered in 2020 following implementation of audio-only prenatal virtual visits did not experience more adverse pregnancy outcomes than women who delivered in 2019."

Pediatrics: [Neonatal SARS-CoV-2 Infections in Breastfeeding Mothers](#) (13 April 2021)

"To assess infection rates predischARGE and postdischarge in breast milk-fed newborns with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive mothers who were separated postdelivery from their mothers and discharged from the hospital. Also, we aim to evaluate breastfeeding rates predischARGE and postdischarge.

Nasopharyngeal swabs for SARS-CoV-2 were obtained from symptomatic and high-risk women in the delivery room. Mothers with positive SARS-CoV-2 test results were separated from the newborns. Newborns were screened within 48 hours of delivery, and anti-infectious guidelines were imparted to the mothers before discharge. Rescreening took place ≥ 14 days postdischarge. Data regarding SARS-CoV-2-positive household members and breastfeeding were obtained by follow-up phone calls.

A total of 73 newborns of SARS-CoV-2-positive mothers were born in Israel during the ~ 3 -month period under study. Overall, 55 participated in this study. All neonates tested negative for the virus postdelivery. A total 74.5% of the neonates were fed unpasteurized expressed breast milk during the postpartum separation until discharge. Eighty-nine percent of the neonates were discharged from the hospital after their mothers were instructed in anti-infection measures. In 40% of the households, there were additional SARS-CoV-2-positive residents. A total of 85% of the newborns were breastfed postdischarge. Results for all 60% of the newborns retested for SARS-CoV-2 postdischarge were negative.

No viral infection was identified in neonates born to and separated from their SARS-CoV-2-positive mothers at birth and subsequently fed unpasteurized breast milk. All infants breastfed at home remained SARS-CoV-2 negative. These findings may provide insights regarding the redundancy of postpartum mother-newborn separation in SARS-CoV-2-positive women and, assuming precautions are adhered to, support the safety of breast milk."

JAMA: [SARS-CoV-2-Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women](#) (12 April 2021)

"This prospective study investigated whether antibodies from SARS-CoV-2 immunization of nursing mothers transferred to infants as a potentially protective effect....

This study found robust secretion of SARS-CoV-2 specific IgA and IgG antibodies in breast milk for 6 weeks after vaccination. IgA secretion was evident as early as 2 weeks after vaccination followed by a spike in IgG after 4 weeks (a week after the second vaccine)."

Pediatric Population

News in Brief

"Hospitals open pediatric long-haul COVID units as children grapple with lingering virus effects" ([CBS](#)).

Doctors warn that they are seeing more self-harm related injuries in children ([WashPo](#)).

Pfizer/BioNTech has requested expansion of the EUA for their COVID-19 vaccine to include adolescents 12-15 years old ([Pfizer \[pdf\]](#)).

"We are turning COVID-19 into a young person's disease: Even as cases drop among vaccinated Americans, the coronavirus still can spread among unvaccinated people—who will be disproportionately children" ([Atlantic](#); see also: [The Urgency of Vaccinating Kids](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Characteristics and Disease Severity of US Children and Adolescents Diagnosed With COVID-19](#) (09 April 2021)

"This cohort study uses data from the Premier Healthcare Database Special COVID-19 Release to assess the association of demographic and clinical characteristics with severe COVID-19 illness among hospitalized US pediatric patients with COVID-19."

Curr Pediatr Rev: [Atypical Manifestations of Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Children: A Review](#) (06 April 2021)

"Background: In December 2019, a local outbreak of pneumonia presented in Wuhan (China), and quickly identified to be caused by a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The disease caused by SARS-CoV-2 was named COVID-19 and was soon declared as pandemic because of the millions of infections and thousands of deaths worldwide. Children infected with SARS-CoV-2 usually develop asymptomatic or mild disease compared to adults. They are also more likely to have atypical and non-specific clinical manifestations than adults.

Methods: A literature search was performed in PubMed and Scopus to summarize the extrapulmonary manifestations of SARS-CoV-2 infection in children since the beginning of the pandemic. Peer-reviewed papers in English were retrieved using the following keywords and combinations: 'pediatric', 'child', 'infant', 'neonate', 'novel coronavirus', 'SARS-CoV-2', 'COVID 19' and 'gastrointestinal', 'renal', 'cardiac', 'dermatologic' or 'ophthalmologic'. We included published case series and case reports providing clinical symptoms and signs in SARS-CoV2 pediatric patients.

Results: Although fever and symptoms of upper respiratory infection are the most frequently presented, a variety of other atypical presentations has also been reported. The clinical spectrum includes dermatological, ophthalmological, neurological, cardiovascular, renal, reproductive, and gastrointestinal presentations. In addition, a rare multi-inflammatory syndrome associated with SARS-CoV-2 infection has been reported in children, often leading to shock requiring inotropic support and mechanical ventilation.

Conclusions: Clinicians need to be aware of the wider range of extrapulmonary atypical manifestations of SARS-CoV-2 infection in children, so that appropriate testing, treatment, and public health measures can be implemented rapidly."

Mental Health and Wellness

News in Brief

Things are really not great right now for folks' mental health – 47% of adults report feeling that work or stress related to the pandemic has had a major or minor impact on them. ([KFF](#)).

"America has pandemic senioritis: Being so close (and yet so far) is a stress all its own" ([Atlantic](#)).

Peer-Reviewed Articles

JAMA Psychiatry: [Association of US Nurse and Physician Occupation With Risk of Suicide](#) (14 April 2021)

"Question: Is the risk of suicide among US nurses and physicians greater than that in the general population?

Findings: In this cohort study using data from 2007 to 2018 that included 2374 nurses, 857 physicians, and 156 141 individuals in the general population (age, ≥30 years), the suicide incidence rates per 100 000 in 2017-2018 among women were 17.1 for nurses, 10.1 for physicians, and 8.6 for the general population, and the suicide incidence rates per 100 000 in 2017-2018 among men were 31.1 for nurses, 31.5 for physicians, and 32.6 for the general population. The suicide risk compared with the general population was significantly increased for nurses but not for physicians.

Meaning: This study suggests that there was a significantly increased suicide risk for the usual occupation of nurse but not for physician."

See also: [editorial](#)

Lancet Psychiatry: [Suicide trends in the early months of the COVID-19 pandemic: an interrupted time-series analysis of preliminary data from 21 countries](#) (13 April 2021)

"We sourced real-time suicide data from countries or areas within countries through a systematic internet search and recourse to our networks and the published literature. Between Sept 1 and Nov 1, 2020, we searched the official websites of these countries' ministries of health, police agencies, and government-run statistics agencies or equivalents, using the translated search terms "suicide" and "cause of death", before broadening the search in an attempt to identify data through other public sources. Data were included from a given country or area if they came from an official government source and were available at a monthly level from at least Jan 1, 2019, to July 31, 2020. Our internet searches were restricted to countries with more than 3 million residents for pragmatic reasons, but we relaxed this rule for countries identified through the literature and our networks. Areas within countries could also be included with populations of less than 3 million. We used an interrupted time-series analysis to model the trend in monthly suicides before COVID-19 (from at least Jan 1, 2019, to March 31, 2020) in each country or area within a country, comparing the expected number of suicides derived from the model with the observed number of suicides in the early months of the pandemic (from April 1 to July 31, 2020, in the primary analysis).

We sourced data from 21 countries (16 high-income and five upper-middle-income countries), including whole-country data in ten countries and data for various areas in 11 countries). Rate ratios (RRs) and 95% CIs based on the observed versus expected numbers of suicides showed no evidence of a significant increase in risk of suicide since the pandemic began in any country or area. There was statistical evidence of a decrease in suicide compared with the expected number in 12 countries or areas: New South Wales, Australia (RR 0.81 [95% CI 0.72–0.91]); Alberta, Canada (0.80 [0.68–0.93]); British Columbia, Canada (0.76 [0.66–0.87]); Chile (0.85 [0.78–0.94]); Leipzig, Germany (0.49 [0.32–0.74]); Japan (0.94 [0.91–0.96]); New Zealand (0.79 [0.68–0.91]); South Korea (0.94 [0.92–0.97]); California, USA (0.90 [0.85–0.95]); Illinois (Cook County), USA (0.79 [0.67–0.93]); Texas (four counties), USA (0.82 [0.68–0.98]); and Ecuador (0.74 [0.67–0.82]).

This is the first study to examine suicides occurring in the context of the COVID-19 pandemic in multiple countries. In high-income and upper-middle-income countries, suicide numbers have remained largely unchanged or declined in the early months of the pandemic compared with the expected levels based on the pre-pandemic period. We need to remain vigilant and be poised to respond if the situation changes as the longer-term mental health and economic effects of the pandemic unfold."

Int J Emerg Med: [Disaster management of the psychological impact of the COVID-19 pandemic](#) (24 March 2021)

"The COVID-19 pandemic has exposed a suboptimal response to this threatening global disaster, including the response to the psychological impact. Both the economic hardship and the continuous media coverage of alarming news have exacerbated this effect which also includes increased domestic violence.

This is a narrative review written by three experts in community medicine, disaster medicine and psychiatry reflecting the interdisciplinary approach in managing disasters. Selected important papers, personal published papers, PUBMED articles and media news related to the disaster management of the psychological effects of COVID-19 pandemic were collected over the last year, critically appraised and used in writing this manuscript.

The COVID-19 pandemic causes major emotional distress. Lack of effective treatments and availability of the current vaccines for this virus increases the fear of being infected and infecting others. Negative emotions are common and are related to adjustment but may progress in the long term to anxiety, depression, and post-traumatic stress syndrome. The COVID-19 pandemic has a major impact on mental health. The most common distress reactions include anxiety, insomnia, perception of insecurity, anger, fear of illness, and risky behaviors. Patients having mental disorders are vulnerable during the pandemic because of (1) somatic vulnerability, (2) cognitive and behavioral vulnerability, (3) psychosocial vulnerability, and (4) disruption to psychiatric care. Psychiatric wards, which are commonly separate from main hospitals, should be included in the disaster management plans. Acute care physicians carry the psychological and ethical impact of difficult triage decisions when ending the support of some patients to save others. A combination of fear and guilt may overcome normal human tolerance levels in vulnerable health workers. The moral injuries can be carried for a long time.

Addressing the psychological effects is an essential component of disaster management of infectious pandemics. This should be implemented through the whole spectrum of disaster management including preparedness, mitigation, response, and recovery."

Ann Emerg Med: [Symptoms of Anxiety, Burnout, and PTSD and the Mitigation Effect of Serologic Testing in Emergency Department Personnel During the COVID-19 Pandemic](#) (04 February 2021)

"Among a comprehensive range of frontline emergency department health care personnel, we assessed symptoms of anxiety and burnout, specific coronavirus disease 2019 (COVID-19) work-related stressors, and risk for post-traumatic stress disorder (PTSD). We also determined whether COVID-19 serologic testing of HCP decreased their self-reported anxiety.

In a prospective cohort study from May 13, 2020, to July 8, 2020, we used electronic surveys to capture participant self-reported symptoms before and after serologic testing for anti-SARS-CoV-2 immunoglobulin G antibodies. Participants were physicians, nurses, advanced practice providers, and nonclinical ED personnel at 20 geographically diverse United States EDs. We evaluated these domains: 1) the effects of the COVID-19 pandemic on overall stress and anxiety; 2) COVID-19-related work stressors; 3) burnout; and 4) PTSD risk (measured using the Primary Care-PTSD Screen for DSM-5, a 5-item screening instrument in which a score of ≥ 3 signifies high risk for PTSD). We also assessed perceptions of whether results of COVID-19 antibody testing decreased participants' self-reported anxiety.

Of 1,606 participants, 100% and 88% responded to the baseline and follow-up surveys, respectively. At baseline, approximately half (46%) reported symptoms of emotional exhaustion and burnout from their work, and 308 (19.2%, 95% confidence interval [CI] 17.3% to 21.1%) respondents screened positive for increased PTSD risk. Female respondents were more likely than males to screen positive (odds ratio [OR] 2.03, 95% CI 1.49 to 2.78). Common concerns included exposing their family and the health of coworkers diagnosed with COVID-19. After receiving antibody test results, 54% (95% CI 51.8 to 56.7) somewhat agreed, agreed, or strongly agreed that knowledge of their immune status had decreased their anxiety. A positive serology result indicating prior SARS-CoV-2 infection was associated with a higher likelihood of reporting decreased anxiety (2.83, 95% CI 1.37 to 5.83).

Symptoms of anxiety and burnout were prevalent across the spectrum of ED staff during the COVID-19 pandemic. One-fifth of ED personnel appeared to be at risk for PTSD. Increased provision of serologic testing may help to mitigate anxiety."

Disparities and Health Equity

News in Brief

The CDC has established a web portal on Racism and Health "to serve as a hub for our activities, promote a public discourse on how racism negatively affects health and communicate potential solutions" ([CDC](#)).

Opinion: "There is a real danger that covid-19 will become entrenched as a disease of poverty" ([BMJ](#)).

Peer-Reviewed Articles

MMWR: [Emergency Department Visits for COVID-19 by Race and Ethnicity — 13 States, October–December 2020](#) (12 April 2021)

"What is already known about this topic? Hispanic, American Indian or Alaska Native, and Black persons have higher rates of hospitalization and death attributable to COVID-19 than do White persons.

What is added by this report? Data from 13 states indicate that compared with White persons, Hispanic and American Indian or Alaska Native persons experienced 1.7 times the rate, and Black persons experienced 1.4 times the rate of emergency department care visits for COVID-19 during October–December 2020.

What are the implications for public health practice? Emergency department COVID-19 visit data can provide insight into ongoing areas of racial/ethnic inequity in health status and disease outcomes and can be used to prioritize prevention resources, including COVID-19 vaccination, to reach disproportionately affected groups."

See also this MMWR article: [Update: COVID-19 Pandemic–Associated Changes in Emergency Department Visits — United States, December 2020–January 2021](#) (16 April 2021)

MMWR: [Trends in Racial and Ethnic Disparities in COVID-19 Hospitalizations, by Region — United States, March–December 2020](#) (12 April 2021)

"What is already known about this topic? COVID-19 disproportionately affects racial and ethnic minority groups in the United States.

What is added by this report? Within each U.S. Census region, the proportion of hospitalized patients with COVID-19 was highest for Hispanic or Latino patients. Racial and ethnic disparities were largest during May–July 2020 and became less pronounced as the pandemic spread throughout the country; however, disparities remained in December 2020 in all regions.

What are the implications for public health practice? Understanding the social determinants of health contributing to geographic and temporal differences in racial and ethnic disparities at a local level can help guide public health prevention strategies and equitable resource allocation, including COVID-19 vaccination, to address COVID-19–related health disparities."

Risk, Transmission, and Exposure

News in Brief

"How safe are you from Covid when you fly?" – a visualization of how air circulates on a plane ([NYT](#); may not work on NMCP network because of style and format).

Environment – factors like sunlight, temperature, or seasons – are not likely to affect transmissibility of SARS-CoV-2 variant B.1.1.7 ([DHS](#); see also: [J Infect Dis article](#)).

We can probably just stop with the 'hygiene theater' ([Atlantic](#); see also: [CDC science brief on fomite transmission](#)).

Commentary: "Ten scientific reasons in support of airborne transmission of SARS-CoV-2" ([Lancet](#)).

Peer-Reviewed Articles

MMWR: [Airport Traveler Testing Program for SARS-CoV-2 — Alaska, June–November 2020](#) (23 April 2021)

"What is already known about this topic? To reduce traveler-related introduction of SARS-CoV-2 into Alaska, the state instituted a traveler testing program in June 2020. Travelers could be tested within 72 hours before arrival or on arrival or could quarantine for 14 days without testing.

What is added by this report? SARS-CoV-2 testing on arrival in Alaska airports identified 951 SARS-CoV-2 infections, or one per 406 arriving travelers, and might have contributed to Alaska's low incidence during the summer by reducing opportunities for community transmission at travelers' destination locations.

What are the implications for public health practice? Posttravel self-quarantine and testing programs might reduce travel-associated SARS-CoV-2 transmission and importation, even without enforcement. Traveler education and community and industry partnerships might help ensure success."

MMWR: [Laboratory Modeling of SARS-CoV-2 Exposure Reduction Through Physically Distanced Seating in Aircraft Cabins Using Bacteriophage Aerosol — November 2020](#) (23 April 2021)

"What is already known about this topic? Aircraft can hold large numbers of persons in close proximity for long periods, which are conditions that can increase the risk for transmitting infectious diseases.

What is added by this report? Based on laboratory modeling of exposure to SARS-CoV-2 on single-aisle and twin-aisle aircraft, exposures in scenarios in which the middle seat was

vacant were reduced by 23% to 57%, compared with full aircraft occupancy, depending upon the model.

What are the implications for public health practice? Physical distancing of airplane passengers, including through policies such as middle seat vacancy, could provide additional reductions in risk for exposure to SARS-CoV-2 on aircraft."

JAMA: [Indoor Air Changes and Potential Implications for SARS-CoV-2 Transmission](#) (16 April 2021)

"This JAMA Insights review summarizes basic measures of indoor air ventilation as a means to explain how increases in frequency of air exchange and filtration capture efficiency could mitigate far-field airborne transmission of SARS-CoV-2 inside rooms and buildings."

JAMA Intern Med: [Fitted Filtration Efficiency of Double Masking During the COVID-19 Pandemic](#) (16 April 2021)

"This quality improvement study compares the fitted filtration efficiency of commonly available face masks worn singly, doubled, or in combinations....

Results of this quality improvement study demonstrated that wearing a medical procedure mask underneath a cloth mask provided the best improvement to FFE of all the combinations evaluated."

Lancet Respir Med: [SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study](#) (15 April 2021)

"Whether young adults who are infected with SARS-CoV-2 are at risk of subsequent infection is uncertain. We investigated the risk of subsequent SARS-CoV-2 infection among young adults seropositive for a previous infection.

This analysis was performed as part of the prospective COVID-19 Health Action Response for Marines study (CHARM). CHARM included predominantly male US Marine recruits, aged 18–20 years, following a 2-week unsupervised quarantine at home. After the home quarantine period, upon arrival at a Marine-supervised 2-week quarantine facility (college campus or hotel), participants were enrolled and were assessed for baseline SARS-CoV-2 IgG seropositivity, defined as a dilution of 1:150 or more on receptor-binding domain and full-length spike protein ELISA. Participants also completed a questionnaire consisting of demographic information, risk factors, reporting of 14 specific COVID-19-related symptoms or any other unspecified symptom, and brief medical history. SARS-CoV-2 infection was assessed by PCR at weeks 0, 1, and 2 of quarantine and participants completed a follow-up questionnaire, which included questions about the same COVID-19-related symptoms since the last study visit. Participants were excluded at this stage if they had a positive PCR test during quarantine. Participants who had three negative swab PCR results during quarantine

and a baseline serum serology test at the beginning of the supervised quarantine that identified them as seronegative or seropositive for SARS-CoV-2 then went on to basic training at Marine Corps Recruit Depot—Parris Island. Three PCR tests were done at weeks 2, 4, and 6 in both seropositive and seronegative groups, along with the follow-up symptom questionnaire and baseline neutralising antibody titres on all subsequently infected seropositive and selected seropositive uninfected participants (prospective study period).

Between May 11, 2020, and Nov 2, 2020, we enrolled 3249 participants, of whom 3168 (98%) continued into the 2-week quarantine period. 3076 (95%) participants, 2825 (92%) of whom were men, were then followed up during the prospective study period after quarantine for 6 weeks. Among 189 seropositive participants, 19 (10%) had at least one positive PCR test for SARS-CoV-2 during the 6-week follow-up (1.1 cases per person-year). In contrast, 1079 (48%) of 2247 seronegative participants tested positive (6.2 cases per person-year). The incidence rate ratio was 0.18 (95% CI 0.11–0.28; $p < 0.001$). Among seropositive recruits, infection was more likely with lower baseline full-length spike protein IgG titres than in those with higher baseline full-length spike protein IgG titres (hazard ratio 0.45 [95% CI 0.32–0.65]; $p < 0.001$). Infected seropositive participants had viral loads that were about 10-times lower than those of infected seronegative participants (ORF1ab gene cycle threshold difference 3.95 [95% CI 1.23–6.67]; $p = 0.004$). Among seropositive participants, baseline neutralising titres were detected in 45 (83%) of 54 uninfected and in six (32%) of 19 infected participants during the 6 weeks of observation (ID50 difference $p < 0.0001$).

Seropositive young adults had about one-fifth the risk of subsequent infection compared with seronegative individuals. Although antibodies induced by initial infection are largely protective, they do not guarantee effective SARS-CoV-2 neutralisation activity or immunity against subsequent infection. These findings might be relevant for optimisation of mass vaccination strategies."

Clin Infect Dis: [Nosocomial outbreak of COVID-19 by possible airborne transmission leading to a superspreading event](#) (14 April 2021)

"Nosocomial outbreaks with superspreading of COVID-19 due to a possible airborne transmission has not been reported.

Epidemiological analysis, environmental samplings, and whole genome sequencing (WGS) were performed for a hospital outbreak.

A superspreading event involving 12 patients and 9 healthcare workers (HCWs) occurred within 4 days in 3 of 6 cubicles at an old-fashioned general ward with no air exhaust built within the cubicles. The environmental contamination by SARS-CoV-2 RNA was significantly higher in air grilles (>2m from patients' head and not reachable by hands) than high-touch clinical surfaces (36.4%, 8/22 vs 3.4%, 1/29, $p = 0.003$). Six (66.7%) of 9 contaminated air

exhaust grilles were located outside patient cubicle. The clinical attack rate of patients was significantly higher than HCWs (15.4%, 12/78 exposed-patients vs 4.6%, 9/195 exposed-HCWs, $p=0.005$). Moreover, clinical attack rate of ward-based HCWs was significantly higher than non-ward-based HCWs (8.1%, 7/68 vs 1.8%, 2/109, $p=0.045$). The episodes (mean \pm S.D) of patient-care duty assignment in the cubicles was significantly higher among infected ward-based HCWs than non-infected ward-based HCWs (6.0 ± 2.4 vs 3.0 ± 2.9 , $p=0.012$) during the outbreak period. The outbreak strains belong to SARS-CoV-2 lineage, B.1.36.27 (GISAID Clade GH) with the unique S-T470N mutation on WGS.

This nosocomial point source superspreading due to possible airborne transmission demonstrated the need for stringent SARS-CoV-2 screening at admission to healthcare facilities and better architectural design of the ventilation system to prevent such outbreaks. Portable high-efficiency particulate filters were installed in each cubicle to improve ventilation before resumption of clinical service."

Infect Control Hosp Epidemiol: [Providing safe care for patients in the coronavirus disease 2019 \(COVID-19\) era: A case series evaluating risk for hospital-associated COVID-19](#) (05 April 2021)

"We evaluated the risk of patients contracting coronavirus disease 2019 (COVID-19) during their hospital stay to inform the safety of hospitalization for a non-COVID-19 indication during this pandemic.

A case series of adult patients hospitalized for 2 or more nights from May 15 to June 15, 2020 at large tertiary-care hospital in the midwestern United States was reviewed. All patients were screened at admission with the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) polymerase chain reaction (PCR) test. Selected adult patients were also tested by IgG serology. After dismissal, patients with negative serology and PCR at admission were asked to undergo repeat serologic testing at 14–21 days after discharge. The primary outcome was healthcare-associated COVID-19 defined as a new positive SARS-CoV-2 PCR test on or after day 4 of hospital stay or within 7 days of hospital dismissal, or seroconversion in patients previously established as seronegative.

Of the 2,068 eligible adult patients, 1,778 (86.0%) completed admission PCR testing, while 1,339 (64.7%) also completed admission serology testing. Of the 1,310 (97.8%) who were both PCR and seronegative, 445 (34.0%) repeated postdischarge serology testing. No healthcare-associated COVID-19 cases were detected during the study period. Of 1,310 eligible PCR and seronegative adults, no patients tested PCR positive during hospital admission (95% confidence interval [CI], 0.0%–0.3%). Of the 445 (34.0%) who completed postdischarge serology testing, no patients seroconverted (0.0%; 95% CI, 0.0%–0.9%).

We found low likelihood of hospital-associated COVID-19 with strict adherence to universal masking, physical distancing, and hand hygiene along with limited visitors and screening of admissions with PCR."

High Alt Med Biol: [Potential Protective Effect from COVID-19 Conferred by Altitude: A Longitudinal Analysis in Peru During Full Lockdown](#) (20 March 2021)

"The COVID-19 pandemic had a delayed onset in America. Despite the time advantage for the implementation of preventative measures to contain its spread, the pandemic followed growth rates that paralleled those observed before in Europe.

To analyze the temporal and geographical distribution of the COVID-19 pandemic at district-level in Perú during the full lockdown period in 2020.

Analysis of publicly available data sets, stratified by altitude and geographical localization. Correlation tests of COVID-19 case and death rates to population prevalence of comorbidities.

We observe a strong protective effect of altitude from COVID-19 mortality in populations located above 2,500 m. We provide evidence that internal migration through a specific land route is a significant factor progressively overriding the protection from COVID-19 afforded by high altitude. This protection is independent of poverty indexes and is inversely correlated with the prevalence of hypertension and hypercholesterolemia.

Long-term adaptation to residency at high altitude may be the third general protective factor from COVID-19 severity and death, after young age and female sex. Multisystemic adaptive traits or acclimatization processes in response to chronic hypobaric hypoxia may explain the apparent protective effect of high altitude from COVID-19 death."

Impact on Healthcare Workers

News in Brief

Long read: "Burned out by the pandemic, 3 in 10 health-care workers consider leaving the profession: After a year of trauma, doctors, nurses and other health workers are struggling to cope" ([WashPo](#)).

Of course, burnout is a problem for clinicians, even outside of pandemic things; spoiler: your gender and work culture aren't doing you any favors ([JAMA Netw Open](#)).

Peer-Reviewed Articles

Clin Infect Dis: [Viral sequencing reveals US healthcare personnel rarely become infected with SARS-CoV-2 through patient contact](#) (15 April 2021)

"Healthcare personnel (HCP) are at increased risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We posit current infection control guidelines generally protect HCP from SARS-CoV-2 infection in a healthcare setting.

In this retrospective case series, we use viral genomics to investigate the likely source of SARS-CoV-2 infection in HCP at a major academic medical institution in the Upper Midwest of the United States between 25 March - 27 December, 2020. We obtain limited epidemiological data through informal interviews and review of the electronic health record. We combine epidemiological information with healthcare-associated viral sequences and with viral sequences collected in the broader community to infer the most likely source of infection in HCP.

We investigated SARS-CoV-2 infection clusters involving 95 HCP and 137 possible patient contact sequences. The majority of HCP infections could not be linked to a patient or co-worker (55/95; 57.9%) and were genetically similar to viruses circulating concurrently in the community. We found 10.5% of infections could be traced to a coworker (10/95). Strikingly, only 4.2% of HCP infections could be traced to a patient source (4/95).

Infections among HCP add further strain to the healthcare system and put patients, HCP, and communities at risk. We found no evidence for healthcare-associated transmission in the majority of HCP infections evaluated here. Though we cannot rule out the possibility of cryptic healthcare-associated transmission, it appears that HCP most commonly becomes infected with SARS-CoV-2 via community exposure. This emphasizes the ongoing importance of mask-wearing, physical distancing, robust testing programs, and rapid distribution of vaccines."

Lancet: [SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study \(SIREN\)](#) (09 April 2021)

"Increased understanding of whether individuals who have recovered from COVID-19 are protected from future SARS-CoV-2 infection is an urgent requirement. We aimed to investigate whether antibodies against SARS-CoV-2 were associated with a decreased risk of symptomatic and asymptomatic reinfection.

A large, multicentre, prospective cohort study was done, with participants recruited from publicly funded hospitals in all regions of England. All health-care workers, support staff, and administrative staff working at hospitals who could remain engaged in follow-up for 12 months were eligible to join The SARS-CoV-2 Immunity and Reinfection Evaluation study. Participants were excluded if they had no PCR tests after enrolment, enrolled after Dec 31, 2020, or had insufficient PCR and antibody data for cohort assignment. Participants attended regular SARS-CoV-2 PCR and antibody testing (every 2–4 weeks) and completed questionnaires every 2 weeks on symptoms and exposures. At enrolment, participants were

assigned to either the positive cohort (antibody positive, or previous positive PCR or antibody test) or negative cohort (antibody negative, no previous positive PCR or antibody test). The primary outcome was a reinfection in the positive cohort or a primary infection in the negative cohort, determined by PCR tests. Potential reinfections were clinically reviewed and classified according to case definitions (confirmed, probable, or possible) and symptom-status, depending on the hierarchy of evidence. Primary infections in the negative cohort were defined as a first positive PCR test and seroconversions were excluded when not associated with a positive PCR test. A proportional hazards frailty model using a Poisson distribution was used to estimate incidence rate ratios (IRR) to compare infection rates in the two cohorts.

From June 18, 2020, to Dec 31, 2020, 30 625 participants were enrolled into the study. 51 participants withdrew from the study, 4913 were excluded, and 25 661 participants (with linked data on antibody and PCR testing) were included in the analysis. Data were extracted from all sources on Feb 5, 2021, and include data up to and including Jan 11, 2021. 155 infections were detected in the baseline positive cohort of 8278 participants, collectively contributing 2 047 113 person-days of follow-up. This compares with 1704 new PCR positive infections in the negative cohort of 17 383 participants, contributing 2 971 436 person-days of follow-up. The incidence density was 7·6 reinfections per 100 000 person-days in the positive cohort, compared with 57·3 primary infections per 100 000 person-days in the negative cohort, between June, 2020, and January, 2021. The adjusted IRR was 0·159 for all reinfections (95% CI 0·13–0·19) compared with PCR-confirmed primary infections. The median interval between primary infection and reinfection was more than 200 days.

A previous history of SARS-CoV-2 infection was associated with an 84% lower risk of infection, with median protective effect observed 7 months following primary infection. This time period is the minimum probable effect because seroconversions were not included. This study shows that previous infection with SARS-CoV-2 induces effective immunity to future infections in most individuals."

Reinfections, Coinfection, and Other Infectious Diseases

News in Brief

Reported cases of sexually transmitted diseases are at an all-time high for the sixth year ([CDC](#)).

Syphilis in particular is bad – especially in folks who use meth ([NPR](#)).

Add the antibiotic pipeline (or lack thereof) to your list of potential worries about treatments for infectious diseases, including multi-drug resistant strains ([CIDRAP](#); see also: [WHO report](#)).

"The flu vanished during COVID. What will its return look like?" ([NYT](#); see also: MMWR: [COVID-19 and Influenza Discharge Diagnoses as a Percentage of Emergency Department \(ED\) Visits, by Year — United States, June 2018–March 2021](#))

Long read: "How COVID hurt the fight against other dangerous diseases: Campaigns to battle tuberculosis, measles and polio have all been set back" ([Nature](#)).

Breakthrough SARS-CoV-2 Infections

"CDC ramps up scrutiny of rare post-vaccination 'breakthrough infections': Experts say the number of people testing positive for the virus after being inoculated is to be expected" ([WashPo](#); see also: [medRxiv preprint](#)).

Peer-Reviewed Articles

JAMA Intern Med: [Incorporating HIV Screening With COVID-19 Testing in an Urban Emergency Department During the Pandemic](#) (12 April 2021)

"This cohort study reports the results of incorporating HIV screening into COVID-19 testing at the University of Chicago emergency department."

Nat Med: [Vaccine development for emerging infectious diseases](#) (12 April 2021)

"Examination of the vaccine strategies and technical platforms used for the COVID-19 pandemic in the context of those used for previous emerging and reemerging infectious diseases and pandemics may offer some mutually beneficial lessons. The unprecedented scale and rapidity of dissemination of recent emerging infectious diseases pose new challenges for vaccine developers, regulators, health authorities and political constituencies. Vaccine manufacturing and distribution are complex and challenging. While speed is essential, clinical development to emergency use authorization and licensure, pharmacovigilance of vaccine safety and surveillance of virus variants are also critical. Access to vaccines and vaccination needs to be prioritized in low- and middle-income countries. The combination of these factors will weigh heavily on the ultimate success of efforts to bring the current and any future emerging infectious disease pandemics to a close."

Statistics

Global

23 APR 2021: 144,878,978 confirmed cases and 3,075,042 deaths in 192 countries/regions

Past Trends

16 APR 2021: 139,244,306 confirmed cases and 2,989,173 deaths

09 APR 2021: 134,102,467 confirmed cases and 2,905,149 deaths

02 APR 2021: 129,761,773 confirmed cases and 2,830,059 deaths

26 MAR 2021: 125,629,394 confirmed cases and 2,757,473 deaths

United States

top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	31,931,027	3,727,913	2,867,831	2,191,038	2,018,044	1,312,620
Deaths	570,357	61,309	49,818	34,696	51,830	24,056

[JHU CSSE](#) as of 1000 EDT 23 April 2021

Virginia

	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	652,321	20,412	10,127	13,566	17,142	8,769	7,743	34,939
Hospitalizations	28,012	956	352	408	954	651	434	1,548
Deaths	10,666	286	171	221	248	187	183	382

[VA DOH](#) as of 1000 EDT 23 April 2021